92, 93, 94, 95, 96, 97, 98, or 99% identical to the VH1 and VL1 CDR sequences of v7091 (SEQ ID NOs 223, 225, 227, 37, 39, and 41), and wherein the VL1 domain comprises 1, 2, 3, 4, or 5 amino acid substitutions and/or the VH1 domain comprises 1, 2, 3, 4, or 5 amino acid substitutions;

a second antigen-binding polypeptide construct which monovalently and specifically binds a HER2 ECD4 (extracellular domain 4) antigen on a HER2-expressing cell;

first and second linker polypeptides, wherein the first linker polypeptide is operably linked to the first antigen-binding polypeptide construct, and the second linker polypeptide is operably linked to the second antigen-binding polypeptide construct;

wherein one or both of the first or the second antigen binding polypeptide construct is an scFv,

wherein the linker polypeptides are capable of forming a covalent linkage with each other, and

wherein tumor growth is decreased as compared to a control receiving an equivalent amount of a non-specific control antibody, as compared to a control receiving an equivalent amount of Herceptin/trastuzumab, or as compared to a control not receiving treatment.

4. The method of any of the above claims, wherein the binding affinity of the antigen binding construct to murine HER2 extracellular domain as measured by surface plasmon resonance (SPR) is greater than the binding affinity of v7091 (SEQ ID NOs 33, 219, and 295) to murine HER2 extracellular domain as measured by surface plasmon resonance (SPR), optionally wherein the antigen binding construct and v7091 bind the same epitope, optionally wherein the antigen binding construct binds the same epitope as pertuzamab, optionally wherein the antigen binding construct has a greater Bmax than v7091, and optionally wherein the antigen binding construct is internalized to a greater extent upon cell surface binding relative to v7091.

5. The method of any of the above claims, wherein the binding affinity of the antigen binding construct to murine HER2 extracellular domain as measured by surface plasmon resonance (SPR) is equal to or greater than the binding affinity of a monospecific anti-HER2 ECD4 antibody (v506; SEQ ID NO:1 and SEQ ID NO:317) to murine HER2 extracellular domain as measured by surface plasmon resonance (SPR).

6. The method of any of the above claims, wherein the first antigen-binding polypeptide construct comprises the VH1 and VL1 CDR sequences of v7091 (SEQ ID NOs 223, 225, 227, 37, 39, and 41), wherein the VL1 domain comprises 1, 2, 3, 4, or 5 amino acid substitutions and/or the VH1 domain comprises 1, 2, 3, 4, or 5 amino acid substitutions, optionally wherein the first antigen-binding polypeptide construct comprises a substitution at Y96 in the VL1 domain (SEQ ID NO:35), optionally wherein the first antigen-binding polypeptide construct comprises a Y96A substitution in the VL1 domain (SEQ ID NO:35), optionally wherein the first antigen-binding polypeptide construct comprises substitutions at T30, A49, and/or L69 in the VH1 domain (SEQ ID NO:221), optionally wherein the first antigen-binding polypeptide construct comprises T30A, A49G, and/or L69F substitution(s) in the VH1 domain (SEQ ID NO:221), and optionally wherein the first antigen-binding polypeptide construct comprises T30A, A49G, and L69F substitution(s) in the VH1 domain (SEQ ID NO:221).

7. The method of any of the above claims, wherein the second antigen-binding polypeptide construct comprises VH2 and VL2 CDR sequences that are at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to the VH2 and VL2 CDR sequences of v10000 (SEQ ID NOs 299, 301, 303, 307, 309, and 311), optionally wherein the second antigen-binding polypeptide construct comprises the VH2 and VL2 CDR sequences of v10000 (SEQ ID NOs 299, 301, 303, 307, 309, and 311).

8. The method of any of the above claims, wherein the antigen binding construct comprises the variable domain sequences set forth in SEQ ID NOs 71 and/or 99, the variable domain sequences set forth in SEQ ID NOs 297 and/or 305, or the variable domain sequences set forth in SEQ ID NOs 71, 99, 297, and 305.

9. The method of any of the above claims, wherein the antigen binding construct comprises the full length sequence set forth in SEQ ID NO 97, the full length sequence set forth in SEQ ID NO 295, the full length sequence set forth in SEQ ID NO 69, or the full length sequences set forth in SEQ ID NOs 97, 295, and 69 (v10000).

10. The method of any of the above claims, wherein the first and second linker polypeptide each comprise an immunoglobulin hinge region polypeptide selected from an IgG1, IgG2 or IgG4 hinge region.

11. The method of any of the above claims, wherein the first and second linker polypeptides are operably linked to a scaffold, optionally an Fc.

12. The method of any of the above claims, wherein the first and second linker polypeptides are operably linked to a dimeric Fc comprising first and second Fc polypeptides each comprising a CH3 sequence, wherein the first Fc polypeptide is operably linked to the first linker polypeptide and the second Fc polypeptide is operably linked to the second linker polypeptide.

13. The method of any of the above claims, wherein (i) the first antigen binding polypeptide construct is an scFv and the second antigen binding polypeptide construct is a Fab; or (ii) the first antigen binding polypeptide construct is a Fab and the second antigen binding polypeptide construct is an scFv; or (iii) both the first antigen binding polypeptide construct and the second antigen binding polypeptide construct are scFvs.

14. The method of any of the above claims, wherein

i. the first antigen-binding polypeptide construct is a Fab and comprises

a. a first heavy chain variable polypeptide VH1 comprising the VH of the pertuzumab arm of v5019, v 5020 v7091, v6717 or v10000 (SEQ ID NOs 221, 149, 221, 259, and 99, respectively), and

b. a first variable light chain polypeptide VL1 comprising the VL of the pertuzumab arm of v5019, v 5020 v7091, v6717 or v10000 (SEQ ID NOs 35, 35, and 71 for v5019, v7091, and v10000, respectively); and

the second antigen-binding polypeptide construct is an scFv and comprises

(a) a second variable heavy chain polypeptide VH2 comprising the VH of the trastuzumab arm of v5019, v 5020 v7091, v6717 or v10000 (SEQ ID NOs 171, 205, 297, 171, and 297, respectively), and

(b) a second variable light chain polypeptide VL2 comprising the VL of the trastzumab arm of v5019, v 5020 v7091, v6717 or v10000 (SEQ ID NO:35 for v5020); or